
بسم الله الرحمن الرحیم

Lupus Nephritis In Renal Transplantation

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Background

Approximately 10 to 30 percent of patients with lupus nephritis (LN) progress to end-stage kidney disease (ESKD), depending upon the severity of the disease, ancestral and socioeconomic factors, nonadherence to treatment, and the response to initial treatment.

Kidney transplantation has been safely performed

in patients with ESKD due to LN and is associated with improved patient survival.

PRETRANSPLANTATION CONSIDERATIONS

1. Timing and Type of Transplantation
2. Immunosuppressive therapy for Antirejection
3. Presence of antiphospholipid antibodies

1 Timing and Type of Transplantation

There are no evidence-based guidelines on how long a patient who has ESKD due to lupus nephritis (LN) should wait prior to kidney transplantation.

It has suggested not setting an arbitrary waiting time on dialysis before transplantation for most patients with SLE.

Patients who have a potential living donor should undergo ***preemptive transplantation*** *provided their extrarenal manifestations of SLE, if present, are deemed stable for surgery.*

Arthritis Care Res (Hoboken). 2015 April ; 67(4): 571–581. doi:10.1002/acr.22482.

Association of Time to Kidney Transplantation with Graft Failure among U.S. Patients with End-Stage Renal Disease Due to Lupus Nephritis

Laura C. Plantinga, ScM[1,2], Rachel E. Patzer, PhD[3,4], Cristina Drenkard, MD, PhD[5], Michael R. Kramer, PhD[1], Mitchel Klein, PhD[1], S. Sam Lim, MD, MPH[5], William M. McClellan, MD, MPH[1], and Stephen O. Pastan, MD[3,6]

an analysis of 4743 patients with ESKD due to LN found that among White patients, those who were transplanted later, compared with those who received a transplant within fewer than three months of dialysis, trended toward an increased risk of graft failure (adjusted hazard ratio [HR] 1.23, 95% CI 0.93-1.63); however, no such association was seen among African-American recipients.

SLE patients with advanced CKD or ESKD who do not have clinically active SLE could be transplanted without a "waiting time" they should be referred for transplant evaluation when their glomerular filtration rate is 20 mL/min or less.

The presence of serologic disease activity at the time of transplantation has not been shown to correlate with transplant outcome.

A systematic literature review and analysis of the Toronto lupus cohort found that the persistence of serologic abnormalities at the time of transplantation was not associated with graft failure.

Seminars in Arthritis and Rheumatism
Volume 46, Issue 6, June 2017, Pages 791-797

The utility of lupus serology in predicting outcomes of renal transplantation in lupus patients: Systematic literature review and analysis of the Toronto lupus cohort ☆

Kristy S. Yap MBBS, FRACP [a],
Murray B. Urowitz MD, FRCPC [a b], Quenby Mahood MI [c],
Jorge Medina-Rosas MD [a], Arthy Sabapathy MHSc [a],
Daeria Lawson HBSc [a], Jiandong Su MSc, BMSc, BSc [a],
Dafna D. Gladman MD, FRCPC [a b],
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https://doi.org/10.1016/j.semarthrit.2016.09.008

Referral and evaluation for kidney transplantation among patients with lupus nephritis-related end-stage kidney disease

Lupus
2023, Vol. 0(0) 1–10

DOI: 10.1177/09612033231219739
journals.sagepub.com/home/lup
Sage

Laura McPherson[1], Laura C Plantinga[2], Penelope P Howards[1], Michael Kramer[1], Stephen O Pastan[3] and Rachel E Patzer[4,5]

2 Immunosuppressive therapy for Antirejection

Induction and maintenance immunosuppressive regimens to prevent rejection are the same among patients with ESKD from LN as among patients with other forms of kidney disease.

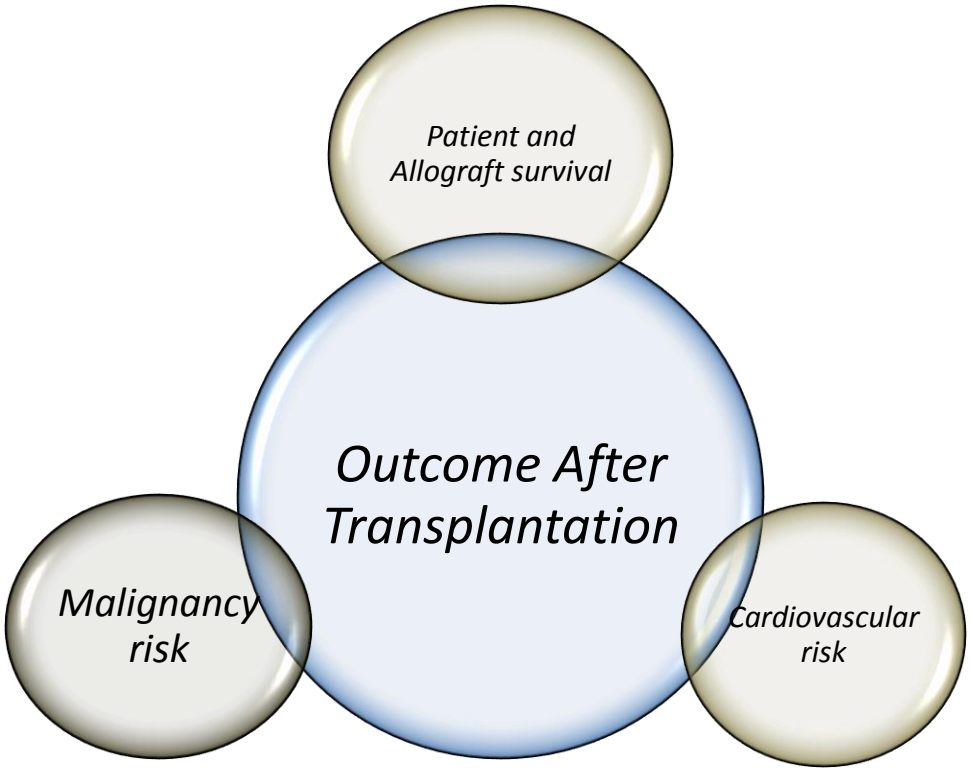
3

Presence of antiphospholipid antibodies

Antiphospholipid antibodies (aPL) are detected in up to 40 percent of patients with SLE . however, the development of antiphospholipid syndrome (APS) is much less common. Nonetheless, patients with SLE who also have aPL are at increased risk for thrombotic events, including the development of thrombotic microangiopathy in the allograft. All patients should be tested for the presence of aPL prior to transplantation.

Patients who develop APS should be treated with anticoagulation.

ASA-Oral Vitamin K-Sirolimus(?)


Patient and
Allograft survival
Outcome After
Transplantation
Malignancy
risk
Cardiovascular
risk

Outcome After Transplantation

Original Research | 22 January 2019

Renal Transplantation and Survival Among Patients With Lupus Nephritis

A Cohort Study

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Author, Article, and Disclosure Information

https://doi.org/10.7326/M18-1570

Patient and Allograft survival

During the study period, 9659 patients with LN-ESRD were waitlisted for a renal transplant, of whom 5738 (59%) had a transplant. Most were female (82%) and nonwhite (60%). Transplant was associated with reduced all-cause mortality (adjusted HR, 0.30 [95% CI, 0.27 to 0.33]) among waitlisted patients. Adjusted HRs for cause-specific mortality were 0.26 (CI, 0.23 to 0.30) for cardiovascular disease, 0.30 (CI, 0.19 to 0.48) for coronary heart disease, 0.41 (CI, 0.32 to 0.52) for infection, and 0.41 (CI, 0.31 to 0.53) for Sepsis.

Outcome After Transplantation

Studies comparing transplant outcomes between patients with ESKD due to LN and those with ESKD due to other kidney diseases have reported mixed results.

Some studies have found higher mortality among patients with LN compared with those with other diseases.

Most, but not all, studies have found that overall 5- and 10-year graft survival rates are similar among patients with LN compared with those in patients with other glomerular diseases.

Outcome After Transplantation

Meta-Analysis > Arthritis Res Ther. 2018 Dec 6;20(1):270. doi: 10.1186/s13075-018-1760-3.

The risks of cancer development in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis

Lebin Song [1], Yi Wang [2], Jiayi Zhang [2], Ninghong Song [2], Xiaoyun Xu [3], Yan Lu [4]

Affiliations + expand

PMID: 30522515 PMCID: PMC6282326 DOI: 10.1186/s13075-018-1760-3

Free PMC article

Malignancy risk

> Lupus Sci Med. 2016 Jun 6;3(1):e000156. doi: 10.1136/lupus-2016-000156. eCollection 2016.

Standardised incidence ratios (SIRs) for cancer after renal transplant in systemic lupus erythematosus (SLE) and non-SLE recipients

Rosalind Ramsey-Goldman [1], Amarpali Brar [2], Carrie Richardson [1], Moro O Salifu [2], Ann Clarke [3], Sasha Bernatsky [4], Dimitre G Stefanov [5], Rahul M Jindal [6]

Affiliations + expand

PMID: 27335659 PMCID: PMC4908873 DOI: 10.1136/lupus-2016-000156

Free PMC article

Outcome After Transplantation

Author manuscript
Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2023 November 01.

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Arthritis Care Res (Hoboken). 2022 November ; 74(11): 1829–1834. doi:10.1002/acr.24725.

Kidney Transplantation and Cardiovascular Events Among Patients with End-Stage Renal Disease due to Lupus Nephritis: A Nationwide Cohort Study

April Jorge, MD[1], Xiaoqing Fu, MPH[1], Claire Cook, MPH[2], Na Lu, MPH[1,2], Yuqing Zhang, DSc[1], Hyon K. Choi, MD, DrPH[1], Zachary S. Wallace, MD, MS[1]

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Cardiovascular risk

RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

One of the most significant concerns in patients with LN who undergo kidney transplantation is whether LN will recur in the allograft.

RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

The exact incidence of recurrent LN has been difficult to establish due to several factors, including the use of light microscopy alone when biopsy is done and short follow-up in many reported studies to detect recurrence.

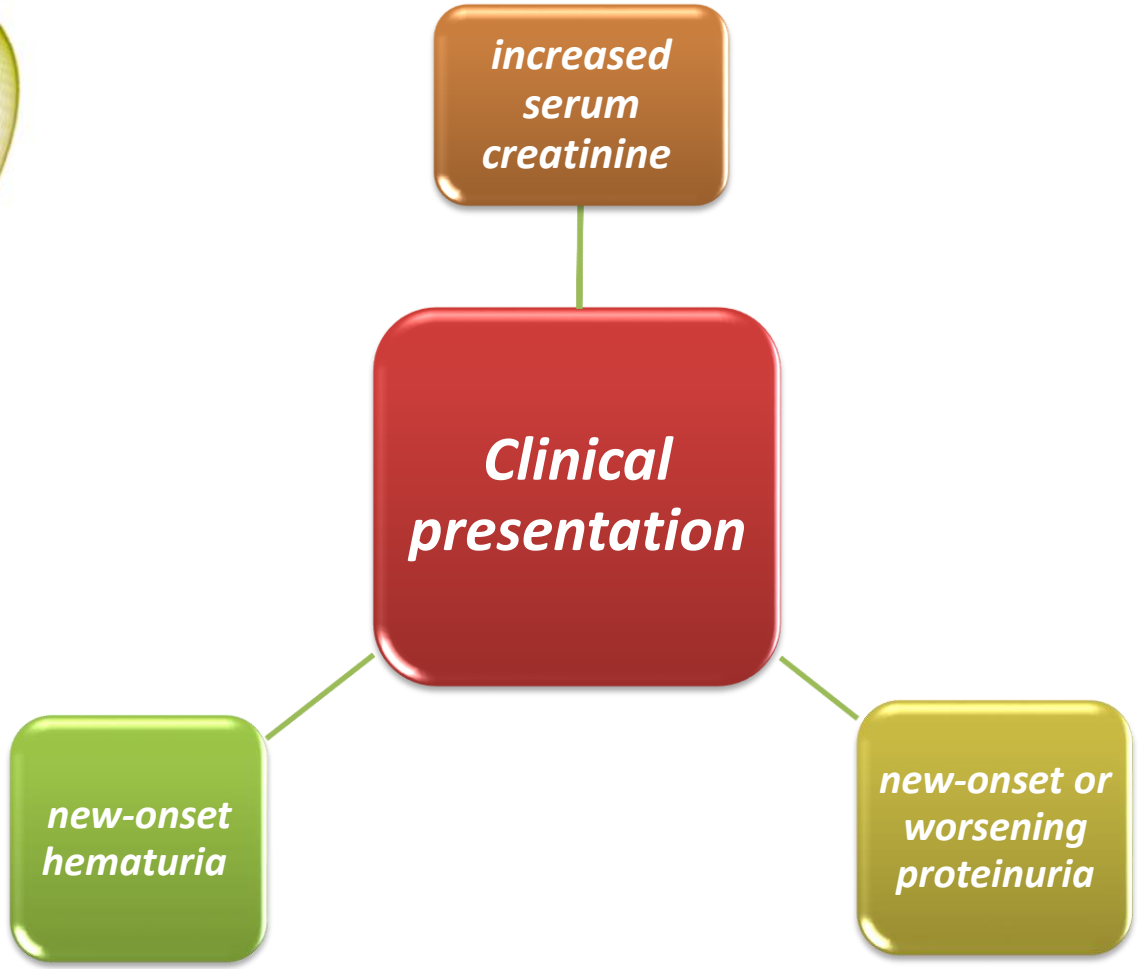
The rate of recurrent LN ranges from 0%to 44% depending on patient characteristics, era of immunosuppression, and indication for renal biopsy , but the incidence of clinically significant recurrent LN in an allograft occurs at ***2-11%.***

RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

Recurrent LN can occur as early as 5 days to 16 years post-transplant,

with median time to recurrence being ***4.3 years*** *post-transplant.*

RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION



RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

Serologic markers such as low complement and high anti-double-stranded DNA (anti-dsDNA) antibody titer have not been found to be reliable predictors of recurrence.

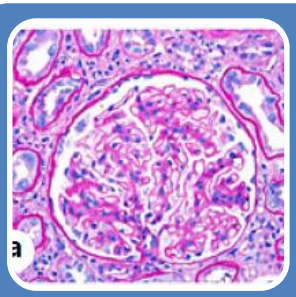
RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

It is imperative to use light microscopy, immunofluorescence, and electron microscopy to diagnose recurrent LN, particularly when there are no obvious clinical manifestations or serological markers suggestive of recurrence.

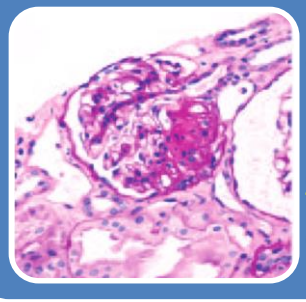
RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION

The histopathologic lesion with recurrent LN may be ***different*** *than that of the native kidney and is* ***usually less severe.***

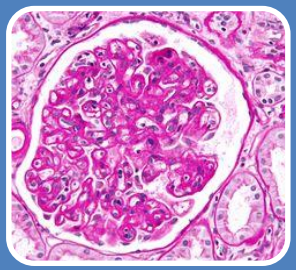
RECURRENT LUPUS NEPHRITIS POSTTRANSPLANTATION



IC-mediated GN with mesangial changes resembling class I and class II Lupus GN,and recurrent membranous GN



atypical lesions consisting of acute proliferative GN and de novo focal segmental glomerulosclerosis each with scant immune deposits



Lesions considered unrelated to SLE, including transplant glomerulopathy and CNI-associated thrombotic microangiopathy

Glomerular Diseases

Review Article

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Recurrent Glomerular Diseases in Renal Transplantation with Focus on Role of Electron Microscopy

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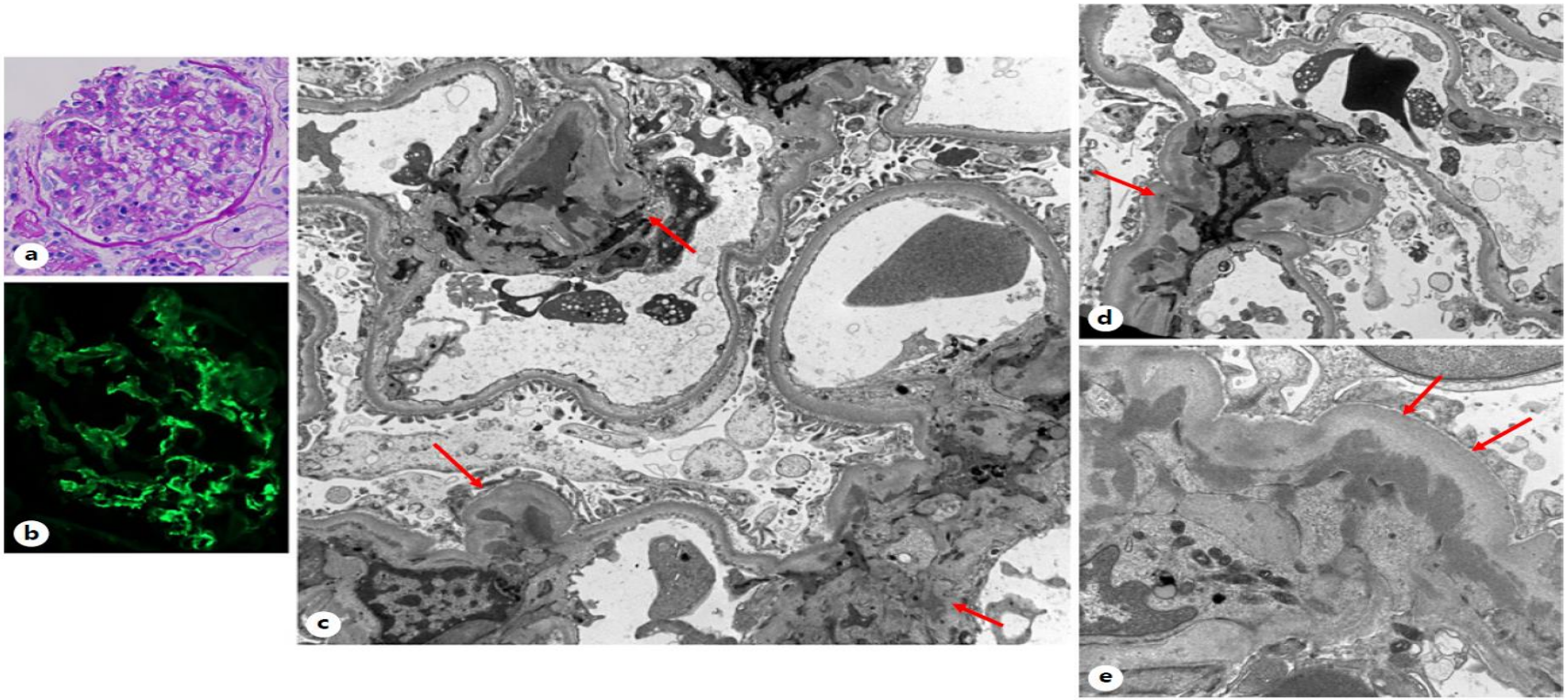

Fig. 10. Recurrent mesangial lupus GN (ISN/RPS class 2). **a** Glomerulus showing mild to moderate mesangial expansion and hypercellularity and normal-appearing peripheral capillaries with patent lumina (PAS, ×400). **b** Granular IgG deposits are found restricted within the glomerular mesangial areas (IgG, ×400). **c–e** Recurrent mesangial lupus glomerulonephritis showing variable amounts of granular dense deposits mainly in the mesangial areas (arrows), while the peripheral capillary basement membranes are of normal thickness and texture with preserved foot processes (×6,000 (**c**), ×6,000 (**d**), ×20,000 (**e**)). GN, glomerulonephritis; PAS, periodic acid-Schiff.

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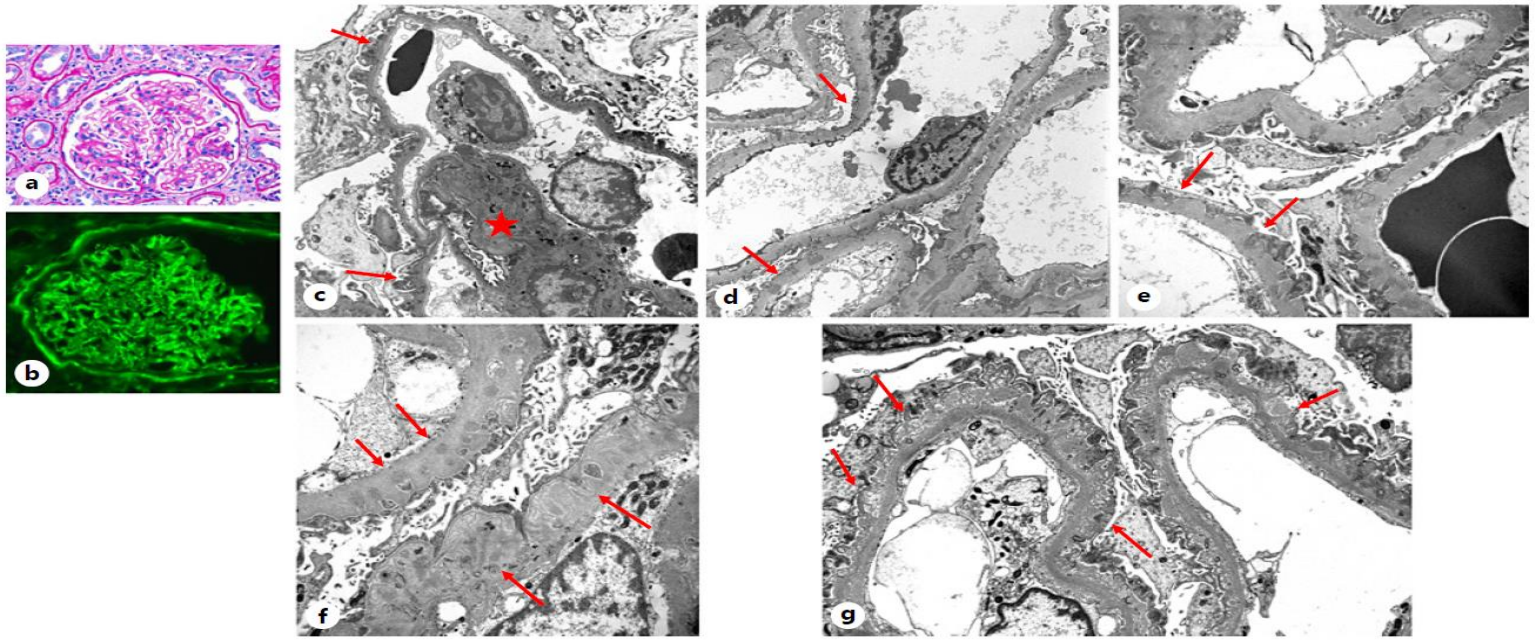

Fig. 11. Recurrent membranous lupus GN (ISN/RPS class 5). **a** Glomerulus displaying focal, mild to moderate mesangial hypercellularity and moderate thickening of the capillary walls with patent lumina, surrounded by mild chronic interstitial inflammation and tubular atrophy (PAS, ×400). **b** The global, granular strong IgG staining along the glomerular capillary walls and mesangial areas (lesser intensity of IgM, IgA, C3, and C1q was also present) (IgG, ×400). **c** A single glomerular capillary loop from an early membranous LN lesion shows small subepithelial electron-dense deposits with rare basement membrane spikes (arrows), localized foot process effacement, and small mesangial deposits (asterisk). No subendothelial deposits are visible (×6,000). **d–f** With disease progression, the glomerular deposits are more numerous with frequent spike formation, partly intramembranous, with occasional evidence of resorption, leaving lucent spaces and accompanied by extensive foot process effacement. The endothelial cells can show segmental or extensive loss of fenestrations and mild swelling (×6,000 (**d**), ×12,000 (**e**), ×12,000 (**f**)). **g** More advanced cases show resolving intramembranous deposits with rarefaction or loose spaces containing small fragments of trapped epithelial cells and persistent foot process distortion or effacement. The lamina densa appears thickened and intact with no evidence of subendothelial deposits (×6,000). GN, glomerulonephritis; PAS, periodic acid-Schiff; LN, lupus nephritis.

Treatment Of Recurrent LN Post-transplant

Treatment Of Recurrent LN Post-transplant

All pts with R.LN

+Proteinuria>500 $\frac{mg}{d}$

+/- HTN

RAS Inhibition Drugs

Treatment Of Recurrent LN Post-transplant

Modification of immunosuppression

*Patients with recurrent LN who have mild lesions (class I or II LN) on allograft biopsy do **not** require a change in the maintenance immunosuppressive regimen used to prevent rejection. Such patients can generally be managed with a RAS inhibitor to reduce proteinuria and control blood pressure.*

Treatment Of Recurrent LN Post-transplant

Pts WITH Recurrent LN(Class III or IV)

escalating the maintenance immunosuppression regimen to treat LN

Options for immunosuppression modification

Increase the dose of MMF to 2000 to 3000 mg/day (or 1440 to 2160 mg/day of EC-MPS).

*If the patient is on **azathioprine**(rather than MMF/EC-MPS), we discontinue azathioprine and switch to MMF or EC-MPS.*

This induction dosing of mycophenolate should be continued for six months before being reduced to conventional maintenance dosing.

Or

*Administer **cyclophosphamide** and discontinue the current antimetabolite (usually MMF/EC-MPS or azathioprine). The optimal cyclophosphamide dose for the transplant recipient is not known, and no studies have examined this issue. Based upon studies of LN in the native kidney and our clinical experience, we use the same regimen as we use in the native kidney. After approximately three to six months, cyclophosphamide is replaced by the **mycophenolate** dose used for transplant rejection prophylaxis, which also serves as ongoing therapy for recurrent LN.*

Options for immunosuppression modification

continue…

Patients who are treated with an increase in the MMF/EC-MPS dose or the addition of ***cyclophosphamide*** *should also be treated with an increase in glucocorticoids. We generally give a pulse of intravenous (IV)* ***methylprednisolone****, usually 250 to 500 mg for one to several days followed by a tapering oral glucocorticoid regimen that, over three to four months, returns to a previous maintenance glucocorticoid dose (eg,* ***prednisone*** *5 mg daily).*

Response to therapy is monitored similarly to that for LN in the native kidney and includes serial evaluation of serum creatinine, proteinuria, and hematuria.

Options for immunosuppression modification

continue…

*If treatment with **mycophenolate** or **cyclophosphamide** is ineffective, some clinicians give **rituximab** in addition to mycophenolate dosed at 2 to 3 g/day, with or without an increase in glucocorticoids.*

There are no published studies that support the use of rituximab for recurrent LN among transplant recipients.

Our approach is based on data supporting the use of rituximab in patients with resistant LN in the native kidney.

Options for immunosuppression modification

continue…

*For recurrent LN in the allograft there are insufficient data to support the addition of either **belimumab** or **voclosporin**, both of which have been approved by the FDA for the treatment of LN.*


THANKS FOR YOUR ATTENTION